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The Hunterian Lectures

ON

RECENT DEVELOPMENTS IN THE RECOGNITION, TREATMENT, AND PROPHYLAXIS OF SYPHILIS

Delivered before the Royal College of Surgeons of England on November 7 and 10, 1911

BY

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LECTURE I.

Delivered on November 7th.

Mr. President, Fellows, and Gentlemen,—In being honoured by the request of your Council to deliver two Hunterian lectures the mind unconsciously turns to the time-honoured name of John Hunter.

Value of Hunter's Observations on Induration.

His demonstration of induration in the syphilitic (Hunterian) chancre in the primary stage, as a clinical sign of early syphilitic infection, is, after the lapse of over a hundred years, a more infallible indication when it exists than a positive Wassermann-Neisser-Brück serum diagnosis reaction. Further, such induration is commonly present when the spirochæta pallida of Schaudinn, discovered in March, 1905, cannot be demonstrated. From time to time persons have attempted to detract from the great value of Hunter's work on syphilis because he erroneously taught that gonorrhœa and syphilis were one and the same disease. Owing to Hunter's initial error we have sometimes been asked to set aside all authoritative teaching. We must not forget, however, that his was necessarily an age of dogmatism, and that other portions of his clinical teaching, like Sir Astley Cooper's classification of dislocations of the hip-joint, have stood the test of time and the judgment of posterity—the best criterion of all good work. As Cicero says, "Men in their lifetime plant trees for another generation to benefit by."

It is not by any means rare to see men or women simultaneously suffering from the two diseases, gonorrhœa and syphilis, and, occasionally, from scabies and non-infecting

chancre in addition. In some instances, before the gonorrhœa resolves, a syphilitic chancre, or even rash, may be developing. I have notes of many such cases. I note in particular a man with gonorrhœa, who developed in hospital a syphilitic chancre in the calf of the left leg with discretely enlarged glands, followed within three months by a roseolar rash.

Another difficult case occurred in association with gonorrhœa where there was a deep-seated indurated mass on the under surface of the penis about an inch from the meatus urinarius. I asked a Fellow of this College kindly to open the abscess. He sent the man off the operating table as he considered that there could be no possible doubt that it was a Hunterian indurated urethral chancre. As urethral syphilitic chancres ordinarily occur at the meatus, and I had seen other cases of this nature, I opened the supposed chancre in his presence, and on deep incision the pus flowed freely from a peri-urethral abscess, and syphilis did not later supervene. Phimosis in association with purulent balanitis may or may not mask an underlying syphilitic ulcer, the real nature of which is only disclosed on operation, or later. The gonococcus may occasionally be demonstrated in a purulent balanitis and no urethral discharge be present.

With such a multiplicity of possible contingencies and no ultra-microscope, Hunter's mistake is excusable. The correctness, however, of the clinical fact of induration in a syphilitic chancre in association with discrete enlargement of adjacent lymphatic glands is a bequest the value of which has been insufficiently realised. At the present time there is a tendency, more especially in dealing with early syphilis, to set on one side valuable clinical facts in favour of bacteriological methods, and to pronounce an infallible verdict on the sole evidence of a Wassermann reaction. This test, in my experience and in that of other persons, may sometimes be negative when constitutional manifestations of syphilis are present, and not infrequently positive in non-syphilitic conditions.

I propose with your kind indulgence to deal with the diagnosis of early syphilis from three points of view: (1) Demonstration of spirochæta pallida of Schaudinn; (2) Wassermann-Neisser-Brück serum diagnosis reaction; and (3) clinical evidence.

I. Demonstration of Spirochæta Pallida.

Major L. W. Harrison, R.A.M.C., at Rochester-row Military Hospital, states that he only succeeded in demonstrating the spirochæta pallida in 152 out of 202 cases of syphilitic sores. He suggests that in the remaining 25 per cent. of cases local antiseptics or other causes may have prevented the demonstration. Another observer found the spirochæta in 35 out of 52

cases of syphilis.[1] It is instructive to realise that local antiseptics have this valuable bactericidal property, which is equally applicable to all stages. Stress was laid by me on this very point 13 years ago, in writing that[2] "The application of the rules of antiseptic, aseptic, and general surgery to the wounds of syphilis is valuable in proportion to the extent and manner in which they are used. It is noticed what extremely successful results follow the removal of the local products of pus formation." Mr. Ernest Lane, referring to the exudate from initial lesions, states: "I have encountered several cases in which the treponema was not discovered after repeated examinations, and in which the case ultimately proved to be one of syphilis." This is a not infrequent experience, and I have seen numerous failures in the hands of skilled and highly trained observers to demonstrate the spirochæta pallida in chancres that were obviously syphilitic. The organism probably lies embedded in fibrous indurations, and in some cases may be demonstrated in sections.

Dr. Reinke, at Wiesbaden in 1910, demonstrated granules in the lung of a child in an autopsy performed after treatment by salvarsan. The granules were derived from spirochæta.[3] Dr. Balfour considers[4] "that granule shedding in treponema pallidum occurs before any treatment of the case is begun. It is, therefore, in all probability a feature in the life-history of the spirochæta. . . . . The same is true of other spirochætes associated with that of syphilis, and is specially well seen in the case of spirochæta refringens. . . . . The granules being of the nature of resistant spores, and so far as those derived from T. pallidum are concerned, doubtless play an important part in relapses and in the later manifestations of syphilitic infections."

The fact that in syphilitic chancres several varieties of spirochætæ exist and naturally shed granules suggests for our consideration whether there is any developmental relationship between these numerous varieties of spirochætæ always found in association in the primary syphilitic chancre. It is only in the blood and under scabs or in lesions of true constitutional syphilis that we find the treponema pallidum apart from other spirochætæ. We have an analogy for such possible development in the case of other organisms, as, for instance, paratyphoid organisms and those of Eberth's bacillus of enteric fever.

Noguchi[5] recently claims "to have made pure cultures of the spirochæta pallida which were pathogenic for the rabbit, and produced diseases identical with those set up by syphilitic material. . . . . Two strains of the spirochæta pallida in pure culture were obtained, and when inoculated into the testicle of the rabbit gave rise to typical lesions containing numerous spirochætes." Other observers point out in this connexion[6] "that experimental investigations in syphilis have become more

general since the demonstration by Tomaczewski of a testicular infection in the rabbit. This animal is more suitable than monkeys on the score of expense, the lesions are well localised for observation and are very rich in spirochætæ. Positive inoculations are readily obtained on the skin of the scrotum or deeply into the testis. Some disadvantage is, however, to be found in the fact that in the rabbit the disease is practically local and liable to spontaneous cure. No generalised symptoms are observed, although the virus is demonstrable in the internal organs by means of inoculations of these organs into other animals." What are we to infer from this? Has the rabbit special properties in its blood which prevent the evolution of external generalised manifestations of syphilis? A principal feature of this disease in man is a repeated and long-continued series of skin and nervous symptoms. Syphilis in man may also undergo spontaneous cure. Hata worked extensively on the rabbit when determining the value of "606." In America the question has arisen whether experiments on herbivorous animals can be fairly contrasted with, or are as conclusive as, those on monkeys or on man?[7]

II. Wassermann Test.

Coming to my second heading—namely, Wassermann serum diagnosis tests—it is proposed to deal with this question from the clinical side, as the purely pathological aspects have already been so ably portrayed last year by Professor Emery in his Hunterian lectures on Immunity Reaction in Diagnosis, especially of Tuberculosis and Syphilis. As laboratory methods and clinical facts relating to the Wassermann test do not always coincide, the results of some Wassermann tests, independently performed on cases under my care by Captain T. H. Gibbon, at the Pathological Laboratory, Malta, may prove of interest.[8] The controls, with few exceptions, were negative in the case of soldiers giving no history of syphilis. In the primary stage the results, in conformity with the experience of others, were not infrequently disappointing. In the secondary stage, however, in cases on their first course of mercurial treatment, or earlier, the results were stated to be positive in 40 out of 43 cases. These were usually men with unquestionable constitutional syphilis, the larger number having been recently placed on the syphilis register.

The reaction was positive in 14 out of 18 cases who were on their second, third, or fourth course of mercurial treatment by injections of intramuscular insoluble grey oil. In one negative case with recent syphilis the man was a heavy drinker. The test was further applied to 36 other cases of men who had completed two years' regular mercurial treatment by the above method; the reaction was positive in 25 out of 36 cases. In

one of the negative cases the man was suffering from mercurial stomatitis. In another negative case gummatous ulceration was actually present.

These results were obtained with Fleming's modification of Wassermann, and, as regards secondary syphilis, compare favourably with those obtained by Wassermann's original method. As regards early syphilis the results are difficult to interpret, and I therefore quote the cases in detail.

Results of Wassermann Reaction in Early Cases.

Case 1.—Lance-Corporal A was admitted on 6/11/09 with a non-infecting chancre, no induration, and suppurating buboes, both inguinal; operation. No mercury given. On 30/11/09 the Wassermann test was "positive." He was discharged hospital on 16/12/09. Syphilis did not later supervene.

Case 2.—Private B was admitted on 22/11/09 with a non-infecting chancre situated on corona glandis. Local treatment; no mercury. On 28/11/09 chancre healed; no evidence of induration. Suppurating left inguinal glands, for which an operation was performed. Wassermann test "positive" on 13/12/09, and "negative" on 26/12/09. Syphilis did not later supervene.

Case 3.—Private C admitted on 11/1/10 to 28/1/10. Small non-indurated ulcer on tip of prepuce, and a suppurating bubo right inguinal glands, which burst on 12/1/10. Local treatment. No mercury. 27/1/10, Wassermann doubtful. Syphilis did not supervene.

Case 4.—Private D was in hospital from 8/11/09 to 23/11/09 with a non-indurated ulcer on the frenum; inguinal glands normal. The Wassermann test was "positive" on 9/12/09. The case, on this sole evidence, was diagnosed syphilis and placed on the syphilis register. The principal medical officer was referred to, and caused the soldier to be medically re-examined by a second medical officer. There was no clinical evidence of syphilis, nor did that disease later supervene. The principal medical officer directed the case to be erased from the syphilis register.

Case 5.—Private E was in hospital 24/8/09–4/9/09. Local treatment; no mercury. The Wassermann test was "positive" on several occasions, the last occasion being 27/11/09. He was placed on the syphilis register on this sole evidence on 31/12/09. There was no clinical evidence of syphilis then or since. The case was similarly dealt with as with case No. 4.

Case 6.—Gunner F, admitted from 3/11/09–25/11/09. No induration of chancre. Inguinal glands: one gland only slightly enlarged as the result of simple inflammatory action, which subsided under local treatment; no mercury. Wassermann "negative" 25/11/09 and "positive" 28/12/09. Syphilis did not supervene.

Case 7.—Private G, admitted from 13/12/09–23/12/09. Slight abrasion, no induration, inguinal glands normal. Local treatment; no mercury. Wassermann "positive" 20/12/09. Syphilis did not supervene.

Case 8.—Private H, admitted 15/12/09–7/1/10. Abrasion glans penis, inguinal glands normal. Local treatment; no mercury. He had also a suspicious unhealthy ulcer on the knuckle, and the lymphatic glands above the elbow on the same side were enlarged but tender. Local treatment; no mercury. Wassermann test "positive." Syphilis did not supervene.

Case 9.—Private I was admitted on 28/11/09 to 31/12/09. Multiple sores, due to secondary inoculation from one near frenum. No induration. Inguinal glands normal. Wassermann test "positive" 31/12/09. Syphilis did not later supervene.

Case 10.—Rifleman J was admitted on 15/9/09–10/11/09. Large ulcer 1 in. long. No induration. Inguinal glands normal. Local treatment; no mercury. Wassermann test "positive" on 28/12/09 and on 31/12/09. Syphilis did not supervene.

Case 11.—Private K, admitted on 13/2/11 with an indurated fissured chancre on dorsal aspect of the roll of prepuce reverted. Large hyperplastic mass superficially suppurating in left inguinal region for which an extensive operation was performed on 22/2/11. On 8/3/11 the Wassermann test was negative. Treatment by mercurial inunctions was resorted to in despite of the test. On 30/3/11 superficial glossitis present, but induration of chancre much reduced. 19/4/11 discharged hospital, to continue mercurial injection treatment as out-patient. In June, 1911, he was re-admitted to hospital with well-marked typical patchy syphilitic alopecia on occiput. Anæmic, no rash to date 1/7/11, when he was discharged hospital.

Value of the Test.

The question of the value of the Wassermann reaction in the diagnosis of early syphilis was raised from the clinical side a year ago. I wrote[9]:—

The test, in the primary period, is unfortunately very uncertain, and not infrequently in my experience when a negative result has been recorded syphilis has later supervened. . . . .

In some ten to twelve instances, recently, at Malta, in which the result was reported to me as positive in cases of chancres, and where mercurial or other treatment was not employed, syphilis did not supervene. The chancre and the glands in these instances were not indurated or discretely enlarged. It may be said that the test was defective. Possibly, but the pathologist obtained 98 per cent. of positive results in secondary cases—that is, after rash had occurred.

In the case of an officer recently who suffered from arteriosclerosis associated with a clear history of antecedent syphilis, the test was strongly positive according to one reliable laboratory opinion in London, and yet three weeks later, without treatment,

a negative result was reported from another laboratory. In other instances the test may be negative, and later positive, or *vice versa*, without any material change in the immediate surroundings of the patient.

The test, therefore, in order to be conclusive, requires to be standardised. In order better to ensure scientific accuracy it might be preferable that the clinical signs should be unknown to the pathologist who performs the test. Such independent results are more convincing.

Following this, another observer from the clinical side states[10]:—

We are not disposed to place too implicit reliance upon the presence or absence of Wassermann's reaction in coming to a diagnosis, for our experience is that perfectly definite cases of syphilis with actual lesions at the time of examination may repeatedly give negative reactions.

Another observer, who has unrivalled opportunities at the London Lock Hospital, both from the clinical and pathological standpoint, stated at the meeting of the British Medical Association this year[11]:—

Let me emphasise once again that a Wassermann reaction in the primary stage of syphilis is valueless, since the moment this reaction becomes positive the secondary or stage of general infection has been reached.

Mr. H. W. Bayly states[12]:—

I have personally examined well over 2000 sera. It seems to me, however, that the most essential of all factors in a comparative test such as this is that all factors except the one to be tested should be constant. With Hecht's, Bauer's, Stern's, or Fleming's technique variants are substituted for constants.

Major L. W. Harrison states:—

In his hands the modification by Stern has given a positive reaction in about 2 per cent. of normal cases. . . . . And gives a positive reaction earlier than the original.

On the foregoing evidence, are we prepared to accept unquestioned the dogmatic bacteriological assertion of Dr. Paul Fildes?[13]—

1. That from a positive finding there is within certain understood limits no appeal; the individual yielding such a result is, again within certain limits, to be regarded as actively syphilitic and must be treated as such.

The same writer further states that—

It is well known that many cases give negative results when obviously syphilitic.

Another bacteriologist, in reviewing a recent work on the subject, states[14] :—

2. A number of the histories failed to convince us of the syphilitic nature of the symptoms. For instance, a case of pernicious anæmia is attributed to syphilis on the grounds of a specific history and a positive Wassermann reaction. In this, and in some other instances, the author seems to have fallen into the error of labelling every lesion syphilitic which coincides with a positive Wassermann reaction with or without a specific history. We are convinced that nothing is more likely to bring the test into discredit than allowing the presence of a positive Wassermann reaction to blind us to possible causes other than syphilis for the symptoms which a patient may display.

Boas[15] emphasises the importance of "carrying out all Wassermann's reactions in a quantitative manner—a method which is impossible in the case of all the ordinary suggested modifications. He obtained much better results with the original test in a quantitative manner, and stated that the Wassermann reaction has not, and will not, obviate the necessity for clinical observation in syphilis."

In a recent leader on the subject in the *British Medical Journal* a writer states[16]: "Even among laboratory workers confusion has arisen by reason of the number of modifications and simplifications of Wassermann's original process. Before we can truly estimate the accuracy and reliability of the test it is essential that the relative merits of the original method and of all modifications should be decided, if necessary, by the establishment of a committee of enquiry."

In addition to a positive Wassermann reaction in the ten cases previously cited of unquestionable non-infecting (soft) chancre at Malta, positive results have also been obtained by other observers in various non-syphilitic conditions, such as gonorrhœa, scarlet fever, yaws (fairly constant), leprosy (very high percentage, especially in the tubercular variety), malaria (35 per cent. before the administration of quinine), puerperal eclampsia, lupus erythematosus, trypanosomiasis, pneumonia, enteric fever, tumours, herpes, aortic disease, relapsing fever (54 per cent.), alopecia areata, in some persons under narcosis and in dead bodies. As regards the latter, of 101 specimens of serum from cadavera 59 (that is, 60 per cent.) gave a positive reaction.[17] Sabouraud of Paris is now of opinion that extensive alopecia areata is more commonly due to syphilis, either acquired or hereditary, than to any other single cause.[18] Du Bois investigated 14 cases of alopecia areata typical in every respect, and in 11 found a positive Wassermann reaction where there were no symptoms of syphilis, hereditary or acquired.[19] Dr. J. H. Sequeira of the London Hospital, in showing a case of alopecia areata in a syphilitic subject at the Dermatological Society of London in July, stated "that he had had a number of cases of

alopecia areata examined by the Wassermann test, but that this was the only instance in which a positive reaction had been obtained."[20]

In latent syphilis where manifestations are absent Boas only obtained 37 per cent. of positive results, as contrasted with 97 in secondary and 95 per cent. in tertiary manifestations.[21] It is interesting to consider what is the meaning of this test? Can it be dependent on an excess of albuminous or other products of disintegration arising from increased metabolism?

Before coming to my final heading and dealing with some clinical aspects in the diagnosis of early syphilis, I propose placing a few specimens on the screen. This is in accordance with the usual custom in order to demonstrate material in the Museum of the College. Owing to a large number of the wax models and paintings being too large for the epidiascope, your indulgence is craved if the choice of material is somewhat limited.

III. Clinical Evidence.

I put the clinical aspect last, but in my opinion it is by no means the least valuable. It does not perhaps glitter like the gold of the spirochætæ, nor sound like the brazen cymbal of a positive Wassermann reaction, but as regards induration in the chancre it has the intrinsic merit of home manufacture. Sir Jonathan Hutchinson states: "If the patient has never had syphilis before, whatever are the characters of any primary sore which he may exhibit, the chances are two to one that the sequel will prove that it contained the germs of true syphilis." Owing to advantage having been taken of this statement by certain persons to unduly extol the claims of several new remedies in the therapeutics of syphilis, I have studied this point closely for many years amongst some thousands of in-patients. In the British army, in England and abroad, where numerous cases of venereal sore come under early notice, soldiers are first treated in hospital. Commencing, however, from September, 1903, men on discharge from hospital remain under continued observation. Exact diagnosis on clinical grounds is thus more feasible than in civil life, where cases are wholly treated as out-patients, where their actions are uncontrolled, and where they commonly communicate disease to others. Relative frequency is dependent on numerous factors, such as epidemicity. Soldiers, more especially in England, may resort to civil practitioners and chemists in order to avoid loss of pay by reason of admission to hospital. No doubt in civil practice many cases are only seen by specialists when there is a strong probability of syphilis.

Character of Venereal Sores and Condition of Glands.

I conducted a close investigation at Cairo amongst 200 consecutive in-patients with venereal sores. The cases on discharge from hospital were kept under prolonged observation. There were 45 cases of syphilis—that is, a relative frequency of 3·5 non-infecting chancres (soft chancres) to 1 of syphilis.[22] Previous and present experience and carefully collected military statistics support this general average.

In 155 out of the above 200 cases the condition was conclusively demonstrated on clinical grounds to be non-infecting chancre (soft chancre). The chancre was not indurated and there were not any discretely enlarged and indurated glands in any of the cases. The lymphatic glands commonly suppurated and were operated on in 41 instances. In 36 out of the 45 cases of syphilis induration in the chancre was detected and the lymphatic glands were typical. Rash was later observed in 41 out of the 45 cases. I left the station before the remaining 4 cases had time to develop a rash, but all four had indurated chancres and discretely enlarged lymphatic glands. Pseudo-chancre induré only occurred twice amongst the 200 cases. There were 7 cases of phagedæna: 4 occurred in syphilis primary, and 3 in non-infecting chancre. The relative frequency, however, is of slight value in arriving at a correct diagnosis, the exact nature of the chancre and the condition of the adjacent lymphatic glands being of the utmost importance as regards diagnosis and treatment. In the foregoing investigation at Cairo, which I have since verified at Woolwich, and again at Malta, induration in some degree was almost invariably present at some time in syphilitic chancres, although it need not necessarily be obvious on the occasion or occasions on which the medical man happens to see the case, since it may have disappeared or may not have developed. The induration should be felt with the fingers. It is due to fibrous tissue with few vessels except on the surface. It is rapidly dissipated by adequate treatment with mercury or with potassium iodide, and is much more marked on the tense corona glandis. It is commonly less marked and frequently overlooked on the frænum. In the soft substance of the glans, or on the external skin of the penis, it may be absent or not appreciable (parchment induration). On the glans a yellow film may form. Induration, with rare exceptions, occurred also in the proximal lymphatic glands in the primary stage, and these were bilaterally enlarged either shortly before or just as the rash came fully out. There was either a discrete bullety enlargement or hyperplastic non-suppurating mass, which rarely ended in suppuration in the case of syphilis, and the amygdaloid or bullet nature of the individual glands could be later made out as the mass slowly subsided under mercurial inunctions. These hyperplastic

mattings in the groin usually resulted from concealment, irritation, and active exercise in the chancre stage, and such causes are apt to induce relapse in syphilitic chancres if the treatment is not sufficiently intensive to remove the induration. In the case of non-infecting sore, suppurating buboes rapidly resulted from concealment or neglect in the initial stages. The adjacent lymphatic glands in some instances may be slightly, temporarily, and painfully enlarged as the result of a non-infecting chancre or from other causes, but such glands commonly subside with rest. The glands in untreated or insufficiently treated syphilis, however, usually persist in despite of rest, become discretely larger, and are commonly painless. An increase of induration in the chancre, or the increasing anæmia of the patient in most untreated cases of syphilis will also put us on our guard until one or other of the classical symptoms of generalisation appears and finally clears the diagnosis.

Pseudo-chancre induré, first described by Professor Fournier in Paris, and also by Sir Jonathan Hutchinson in this country, is a condition where induration is stated to occur in a chancre which is non-syphilitic. The fact of the nearest lymphatic glands being normal will usually clear the diagnosis. It is feasible that in some instances such a condition may occur from reinfection in a person already the subject of constitutional syphilis, being, in fact, a local inflammatory reaction.

Various Points in Diagnosis.

Acquired syphilis on the genitals is nearly always accompanied by ulceration, and in certain phases of the ulcer it is quite impossible from the local appearance to diagnose syphilis. Induration may occur early or late in the base or edges of the ulcer, but when slight may escape our vigilance. In the case of artificially inoculated syphilis on the skin by vaccination or otherwise, a papule is the usual initial lesion, and in rare instances I have seen such occur on the glans penis. The vast majority of syphilitic ulcers, however, probably come under the category of so-called "mixed" infections, in which the bacillus of Ducrey or other organisms exist simultaneously with the spirochæta pallida. The ulceration, purulent products, and, in phagedæna, the active necrosis or even sloughing of tissue, are mainly dependent on accidental factors, such as neglect, exercise, and the irritation of a tense prepuce. It can therefore be readily understood why suppurating buboes may occur in connexion with syphilis. Scars on the penis are very dangerous criteria on which to diagnosis syphilis, as the largest scars are often due to loss of substance in a non-infecting chancre with phagedæna. Scars on the penis without any collateral evidence were formerly accepted as strongly suggestive of syphilis by

writers on nervous diseases, but statistics compiled on such slender data should be rejected. Both non-infecting and infecting chancres may be indolent in healing, and the incidence of appearance after exposure to contagion is frequently a doubtful criterion on which to base a diagnosis, since truthful histories are hard to elicit and syphilitic chancres are commonly due to "mixed infections." The time limits were worked out many years ago on experimental or vaccinal inoculations, being 10 to 40 days, with an average of 25 days. Although a syphilitic chancre is in the large majority of instances single, yet the non-infecting variety of chancre also frequently appears single, more especially in hospital, where auto-inoculation has been prevented by aseptic or antiseptic treatment. Amongst patients presenting multiple sores, balanitic excoriations, or abrasions, one of these may later prove to be syphilitic, or a ring of induration may develop from the whole excoriated surface. Urethral chancres usually occur at the meatus with urethral discharge, and may prove to be erosive in nature; induration occurs in most cases as the ulcer heals, and both chains of inguinal glands are usually implicated. Erratic chancres are rare in England and usually syphilitic. In France, Germany, and Denmark extra-genital chancres are stated to occur in 5 per cent. of cases [23]; as far as army practice is concerned probably 1 per cent. The most common situations are the lip and tonsil. I have seen one, however, in the centre of the forehead, and one on the calf of the leg. The nearest lymphatic glands when the chancre is situated on the face are commonly ultra-typically enlarged.

Because a chancre is erratic it is not *ipso facto* syphilitic, although more commonly it is so. Non-infecting like syphilitic chancres may occur on any part of the body, and phagedæna may supervene in either. I have seen a non-infecting chancre on the finger and syphilis did not supervene (Case 8). Wax models of this condition are shown in the St. Louis Hospital Museum. There is also a specimen of a non-infecting ulcer in the groin in which phagedæna supervened. I have seen an unusually severe case of this condition which spread from the groin over the buttocks and between the legs—so-called "creeping bubo" of old works on surgery. They may spread all over the body. In the case in question the man was in hospital under observation over a year. The condition appeared at first sight to be a tertiary syphilitic ulceration in which phagedæna was occurring. There was, however, no clinical evidence of syphilis—the patient was about 20 years old—and syphilitic remedies were absolutely unavailing. The condition eventually resolved under local remedies and baths.

The period of time from contagion until generalisation occurs is a more or less constant factor. It is stated in the Regulations for Army Medical Services that after two months a case of "venereal sore" is to be diagnosed "soft chancre." If syphilis

later occurs it will be dealt with as disease supervening. This point is one of great practical importance at the moment, more especially in the Services, because numerous persons have claimed to abort syphilis, and others have claimed to first cure and then re-inoculate it. From an army statistical point of view it would appear more rational to wait longer and definitely decide the diagnosis, as thereby one instead of two diseases is shown in the returns. The period of time, in my experience, in which generalisation takes place (as evidenced by rash or sore-throat) is 12 to 16 weeks from the date of contagion. The rash or other symptoms, as the result of treatment, may in some instances be latent and not be manifest for a longer period than four months, according to the intensive nature and value of particular forms of treatment. In other cases early syphilis may have been unrecognised and untreated, and mild varieties of rash may come and go in a few days. In such cases the patient commonly presents himself with intense general adenitis, albuminuria, iritis, or other severe manifestations of syphilis.

In conclusion, therefore, the diagnosis of early syphilis would not always appear to be as simple as many persons would have us believe. We naturally wish to prevent as far as possible the later occurrence of tertiary, malignant, and parasyphilitic conditions. In order to obviate these grave conditions it is requisite to both diagnose and treat syphilis early. Whatever each individual may think about the relative significance of Wassermann reactions, the fact must be admitted that in many instances we are as dependent to-day on a correct clinical interpretation of what we see as in the past when John Hunter wrote.

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LECTURE II.

Delivered on November 10th.

Mr. President, Fellows, and Gentlemen,—In my first lecture I dealt with the diagnosis of syphilis, and in this it is proposed to deal with treatment.

Abortive Treatment.

Persons conversant with early syphilis require to know two clinical facts if the spirochæta pallida is not definitely demonstrated—namely, Was induration present in the chancre? Were the adjacent lymphatic glands discretely enlarged? In untreated syphilis the number of cases where these two signs do not exist is very small; so that when they co-exist treatment is fully justified. Otherwise we should always wait for more definite evidence of the disease. The Wassermann reaction, unfortunately, does not help us much in the primary stage. The alleged abortive cure of syphilis in the primary stage by excising chancres, or treatment by new drugs, such as hectine and salvarsan, requires to be received with very considerable caution and closely examined. The so-called primary stage varies in different countries and with different observers. Results are not infrequently worked out on the relative frequency of syphilis occurring in a consecutive series of all venereal sores, but this is obviously fallacious. In the last 100 cases of untreated venereal sores occurring at Malta not 10 per cent. were syphilis. During two months two years ago the bulk of venereal sores were syphilis. Relative incidence is largely dependent on the value of control at the source.

A statement from the bacteriological side was recently made[1] that "during the past 15 months about 300 cases have been treated with salvarsan. . . . . The number of cases in which the only clinical evidence of infection was the primary sore is 22. . . . . In none of the 22 cases has any symptom appeared since the treatment." It is further stated by the same writer that "treatment should be begun as soon as possible where there is the suggestion of a primary syphilitic lesion; even if spirochætæ cannot be found and the serum reaction is negative, treatment should be begun without delay." I merely mention this example, as such premature claims to abort syphilis are of not infrequent occurrence. To pursue such a policy on insufficient evidence does not further the best interests of accurate diagnosis, and the confidence of the patient may be destroyed.

Arsenical Compounds.

Dr. Hallopeau (France), using hectine (benzol-sulphone-para-amino-phenol arsenate of sodium) (containing 21 per cent. of arsenic) recently claims to have aborted syphilis in five out of six cases when the drug was locally used in the sheath of the penis in combination with mercurial and potassium iodide treatment. He states "that the time has arrived to treat syphilis by 30 daily injections of hectine" and he does not hesitate under these conditions to "allow marriage immediately to syphilitics who have followed this cure." By the courtesy of the French colonial authorities at Tunis a supply of hectine was recently sent to Malta for my use. Owing, however, to careful diagnosis on the lines previously mentioned, to the continued use of mercury, and to local preventive measures, early syphilis, as will be later explained, has been entirely stamped out in Malta this year, and in a garrison of 7000 troops there was no primary syphilitic case to try the new remedy on. Dr. Hallopeau also recently states "that iodide of potassium, in opposition to the generally received opinion, exerts a well-marked effect on the chancre."

Without claiming any originality in the matter, this marked effect on the chancre and lymphatic glands was pointed out in this country, and also in Italy 14 years ago,[2] and again 8 years ago;[3] but, like inorganic or organic arsenic in average cases of early syphilis, I do not at this stage pin my faith on potassium iodide as on mercury as a real curative agent, although it is potent in the removal of induration. Iodide of potassium, like salvarsan, is a good cicatrising agent, and has a powerful action on tissue metabolism, and is therefore capable of promoting the absorption of granulation tissue before its conversion into unalterable fibroid tissue. This would *ipso facto* allow local applications and bactericidal agents normally present in blood to have freer access to the spirochætæ. Mercurial inunction applied nightly to large indurations can effect a similar result and expedite local resolution. This local treatment and reduction of induration in the chancre is very important, and without doubt minimises the occurrence of relapsed chancres. It assists other medication to attack the spirochætæ embedded in fibrous tissue, and if "granule shedding" can "naturally" occur in spirochætæ local recrudescences of the chancre are thus explicable when treatment, local and constitutional, is not sufficiently intensive. It is necessary, however, to distinguish between aborting and modifying syphilis. Sir Jonathan Hutchinson has repeatedly pointed out that mercury administered in the primary stage in the manner recommended by him can effectually modify syphilis in many but not in all cases. He writes: "I never expect to see secondary symptoms now if I have seen the case before we begin."[4] It is common knowledge

that if we push mercury in the first three months from contagion the patient declines in many instances to believe he has had syphilis because the secondary symptoms are so modified.

Salvarsan.

Dr. Levy-Bing, whose work I saw in Paris a month ago, and who has given over 500 injections of salvarsan intramuscularly and intravenously, informs me that in the numerous cases in which he has tried it salvarsan does not ever abort syphilis even when given in four weekly doses of 0·6 gramme in the primary stage. Further, that nervous affections and severe relapse are very common six to seven months later, unless mercury is also prescribed. He mentioned two recent cases where meningitis, facial paralysis, and extensive skin eruptions had shortly appeared from his omitting to follow up the salvarsan with mercury. Dr. Levy-Bing speaks not only from the clinical but from the pathological point of view. He uses the ultra-microscope and performs a Wassermann test every two months. He finds that salvarsan in some instances produces a negative Wassermann test more quickly than mercury, but that it rapidly becomes positive again.

Mr. McDonagh states that he has "had 3 cases within the last 12 months of men early in the secondary stage cured by salvarsan return with a diffuse macular rash . . . . which appeared a few weeks after the patient noticed the site of his original sore swell and become red." He considers that this certainly speaks for the efficacy of salvarsan, and states that "within the short time it has been in use already 7 cases of an undoubted re-infection have been reported." In the army such cases have not been regarded as cures or as re-infections, but are usually marked "relapse" in the syphilis register and sent into hospital for more intense and thorough treatment. Without in any way wishing to detract from the undoubted value of salvarsan in certain phases of syphilis, it is noticeable that in early syphilis, after using soamin and arsacetin, a similar condition of affairs occurred. There was marked temporary improvement and a gain in weight, but permanent benefit did not accrue, and relapses were early and severe. It is only three years ago that we were informed that[5] "Injections of soamin can be looked on as prophylactic in the majority of cases against any further development of the disease if given early and in sufficient quantities." On the evidence of cases treated at Woolwich I disputed this view at the time.[6] Eighteen months later, in March, 1910, an expert medical committee at the War Office stated as a result of impartial evidence collected from six large stations, "that the utility of these preparations (arylarsenates)

as a prophylactic against syphilis has not been proved, and does not recommend their administration for that purpose."

There is abundant evidence to show that, like the arylarsenates, the claim of salvarsan to abort syphilis has not been substantiated. Applied locally it acts like a caustic and expedites healing of the chancre in early syphilis, but other forms of local treatment have also this effect. It is useful to inject salvarsan early to expedite the healing of primary lesions, especially amongst prostitute women, and rapidly follow this up with our *pièce de résistance*—mercury—as the real curative agent.

Local Treatment.

Metchnikoff claims to have successfully inoculated the treponema pallidum and prevented syphilis by the early application within 24 hours from contagion of an ointment of calomel 10 parts and lanoline 20 parts. The use of soap or vaseline prior to coitus and washing with any antiseptic lotions immediately afterwards are also of great prophylactic value, and have been long recognised. Any oily substance would tend to block the minute orifices by which the micro-organisms gain an entry, and also tend to lessen the risk of abrasions caused by coitus. Cauterisation rapidly converts an unhealthy sore into a healing ulcer, stops phagedæna, tends to limit bubo formation, and expedites recovery. The application of a caustic does not in reality alter the nature of an infecting sore, and the condition of the adjacent lymphatics nearly always comes to our rescue. Further a rash occurs in syphilis, whether the chancre is cauterised or not. I consider that non-infecting sores (soft chancres), if unhealthy-looking or discharging, should be touched with pure carbolic acid, which is comparatively painless, on admission and every third day, according to the indication of the particular case. Chancres, unless phagedænic, need not be touched if indurated and not ulcerated, or if they bleed profusely before and after touching, since such bleeding, as in simple inflammation, is a sign of commencing resolution. Many writers have advised the withholding of mercury in cases of phagedæna. I admit that caution and judgment are necessary. Local treatment by nitric in preference to carbolic acid, free exposure, prolonged baths, diet, and stimulants ordinarily suffice for phagedænic ulcers, except when the nearest glands are typical of syphilis, when mercurial inunctions should be used. A lowering treatment would have an unquestionably bad effect, whether dietetic or medicinal, especially if mercury is given when syphilis is non-existent.

Mercurial Treatment.

During the past 18 years my work has been almost exclusively confined to treating venereal diseases in large military stations at home and abroad. During this period I have extensively tried most of the recognised modes of mercurial administration, by the mouth, by inunctions, by injections, and by calomel vapour baths.

In the army, in the case of in-patients who are necessarily in hospital in the chancre and rash stage, we are chiefly concerned in trying to arrive at what best holds the syphilis in check. In the garrison of Woolwich in the year 1904 intramuscular injections of insoluble grey oil were ordinarily used for in-patients, and the inauguration of the out-patient system throughout the army dated from January of that year. In 1904 there were 331 admissions for syphilis, the average number of men constantly daily sick in hospital throughout the year with syphilis being 56. In October, 1905, inunctions of ung. hydrarg. and baths were commenced for in-patients, weekly grey oil injections being reserved for out-patients. There was a steady decrease in syphilis. In 1908 there were 53 admissions for syphilis, the average number constantly sick in hospital being only six. The following table shows these facts at a glance for the years 1904-1908 : —

Table I.—*Syphilis : In-patients, Woolwich.*

Year.	Average daily strength of garrison.	Admissions : actual number.	"Constantly sick" : actual number.	Ratio per 1000.	
				Admissions.	Constantly sick.
1904	5311	331	56	62·32	10·70
1905	4966	202	30	41·49	6·14
1906	5096	129	14	15·12	2·72
1907	4702	87	13	18·50	2·71
1908	5666	53	6	8·75	1·28

In 1904 grey oil intramuscular mercurial injections for in-patients and out-patients. In 1905–08 mercurial inunctions for in-patients—injections for out-patients.

I now come to the question of relapse. In Malta, in December, 1909, in a garrison of 6300 soldiers there were 171 cases remaining on the syphilis register under treatment by mercury, first as in-patients and later as out-patients, for

syphilis, and out of these 31 suffered from relapse during the year 1909. In December, 1910, in a garrison of 6800 soldiers, there were 160 cases of syphilis remaining under mercurial treatment, with 21 relapses during the year 1910. These figures for relapse cases for the years 1909-1910 at Malta included men developing tertiary or other late manifestations of syphilis 5 to 10 years after contracting the disease. These figures embraced numerous transfers from other stations, foreign and home. Some of them were severe cases in men suffering from malaria, or the effects of tropical stations. Relapses were very unusual early in the disease. Syphilis cases in Malta, as at Woolwich, are ordinarily treated by inunctions of mercury in hospital in the primary and early secondary stage, and later, for military convenience, by injections of grey oil for out-patients. In 1911 the results are still better, and in a garrison of 7000 troops there is only one case of syphilis at present in hospital (a recent arrival with a severe throat relapse under salvarsan). There are 160 syphilis cases on the register doing their full duty free from any external manifestation of the disease. These figures compare favourably with those of any garrison in the world, and are a lasting tribute to the judicious use of mercury. Time prevents my dealing more fully with the clinical aspects of the relative merits of various modes of administration of mercury. They have received a great deal of attention lately.[7]

Effects of Treatment on the Wassermann Reaction.

To turn to the pathological aspect. We were asked to accept the Wassermann test as the real arbiter of the value of the various methods of administration of mercury and salvarsan. We will see, therefore, what recent reports tell us on these important points.

Mr. H. W. Bayly, pathologist London Lock Hospital, states that "82 per cent. of cases treated by inunction and 35 per cent. of cases treated by injection showed some effect of treatment after only three months." As far as he has gone, therefore, his conclusion is that inunction is the best form of administration of mercury, and he further gathers that Mr. McDonagh's large continental experience leads him also to this opinion. "Calomel injection seems much better than pill treatment, but not so good as inunction, as estimated by the Wassermann reaction. Potassium iodide and the arylarsenates have no effect on the Wassermann reaction, as far as three months' treatment is concerned." Neisser finds that iodide of potassium has an action on the Wassermann reaction.

At a meeting of the British Medical Association in 1910 Mr. McDonagh (London Lock Hospital) stated that "a patient should, before the disease has become generalised, receive the

most active and vigorous form of treatment possible. Mercury, in the form of inunctions, is more potent in this respect than when given in any other form." Working at the Wassermann reaction on the continent he found that it was "almost a rule to obtain a 'negative' reaction after a patient had had a course of inunctions, or less frequently injections." As this bacteriologist has applied the Wassermann test in over 5000 cases his words carry very great weight, and he speaks from the clinical as well as from the pathological point of view.

Taking the Wassermann reaction as our test, Table II. indicates the ultimate effect on syphilis after a year, as distinguished from the immediate effect. Mercurial insoluble injections are contrasted with salvarsan injections on the Wassermann original reaction. The figures are some of those published by Major L. W. Harrison, who has probably done more research work on these points than any one else in this country.[8]

Table II.

Tested after—	Results obtained by Wassermann's original test.		
	Total cases.	Positive.	Negative.
End of third course of mercurial injections (11th month). 14 injections in all given	79	42	37
End of fourth course of mercurial injections (15th month). 18 injections in all given	101	32	69
Three to 11 months after the last injection of salvarsan	99	33	66

Judging from this table it would seem that after a period of about one year from contagion mercurial insoluble injection appears to be as efficacious as salvarsan as judged by Wassermann's original test, which is considered to be the standard. The course of mercurial injections employed, however, was extremely mild, and is recently obsolete in the army. A more intensive early course was introduced two years ago, and this may be productive of better results in future. Major Harrison states that "possibly injections may not be the best form in which to administer mercury." If so, it would appear wiser to test other mercurial methods before discarding them. Inunctions

thoroughly applied in early syphilis appear to have a much greater effect on the Wassermann reaction.

Amongst a further series of 129 cases tabulated at the same time, in which salvarsan was used when mercury is reported to have failed,[9] it is observed that mercurial inunctions were only used in 8 instances, and merely as part of a mixed treatment in which inunctions took a minor share. There were 35 tertiary, malignant, parasyphilitic, or brain syphilis cases. These were unusually severe cases selected from other stations or those in which certain methods other than inunction had failed.

It is interesting to note in this connexion that Professor Fournier's valuable statistics on tabes in 1891 were based on "mercurial" methods other than injection.[10] He gives the statistics of 321 cases of tabes thus: 15 cases, no treatment; 8, potassium iodide, no mercury; 285 were treated by mercury, or more often a combination of mercury and iodide. Of these 285 cases, 70 were treated from a few days to two months, 108 from three to six months, 51 from seven to 12 months, 23 about 12 months, 20 from one to two years, 5 from two to three years, 6 for three years, and 2 for four years.

Sir David Ferrier says that "these statistics favour the view that a still more thorough and effective treatment might prevent the development of tabes altogether. . . . . As regards salvarsan we had better 'wait and see.'"

Salvarsan was only placed on the market in December, 1910, and has not been issued for use to troops at Malta, so I am obliged to quote from the experiences of others. Major Harrison, in London, who received a free issue in July, 1910, had 18 clinical relapses amongst 115 cases of syphilis. In 31 instances the Wassermann test became negative after the use of salvarsan, but returned to positive. This occurred within a period of 3 to 11 months. Cases were selected for salvarsan treatment which had at least one year to serve. The results, therefore, on clinical grounds, if we accept relapses as our test, are apparently no better than with mercury.

Dr. Karl Lange[11] summarises the results of Wassermann reaction after salvarsan treatment in 268 cases of syphilis representing more than 2000 determinations at the Rudolf Virchow Infirmary. Eighteen cases, including one case of malignant syphilis and one of tabes, were negative before treatment. Nine cases were also negative where mercury had been used previously to salvarsan, and remained negative after salvarsan. Two cases of primary sore injected during exhibition of negative Wassermann also remained negative. Five cases of tertiary syphilis became positive after injection, and one died with a positive reaction. Ninety-seven cases remained positive after the salvarsan injection, of which 54 were absolutely unaltered. Amongst these, two adults and six children died during the positive period, although in these cases the degree of

reaction had been partially reduced before death. Thirty-four cases exhibited a distinct reduction in the positive reaction during a period of observation extending over five weeks, but did not become negative. One case of severe laryngeal syphilis exhibited a strongly positive reaction for six weeks in spite of repeated injections of salvarsan. Neisser found that in only 10 per cent. of cases treated by salvarsan a positive Wassermann was changed to negative, and he pointed out that "the reaction cannot decide whether the cure is permanent or not." He pleads for "a combined treatment with these injections and mercury or iodide of potassium," and recommends the use of mercury for three years. Professor Werther, who has treated some 350 cases with salvarsan, states that "in cases treated by him in October, 1910, only 12 per cent. gave a negative Wassermann. . . . . The combination of mercury with salvarsan has a more rapid effect on the reaction than a second dose of salvarsan." Professor Ehrlich states that "in some cases a negative reaction may be present, but after an injection of "606" the reaction becomes positive." If this is so, one naturally asks what is the potential value of a Wassermann test in syphilis, as the figures of Dr. Karl Lange previously quoted, and those of numerous other independent observers, indicate that a large bulk of the cases remain positive, whereas with mercurial inunctions they have been proved to become negative. One assumes that to obtain a negative reaction is the object of the Wassermann test and our guide to the relative therapeutic value of the remedy. This is the usual criterion of all pathological reports when attempts are made to assert the superiority of salvarsan over mercury.

As regards mixed treatment by salvarsan and then mercury and iodide of potassium, a similar plea was put forward with atoxyl, soamin, and arsacetin; and atoxylate of mercury was later evolved by Uhlenhuth which has proved of very little use. Dr. G. Pernet refers to "therapeutic rockets which come down like sticks," and Mr. C. F. Marshall considers that an "attempt is made to break the fall of salvarsan by a parachute of mercury and iodides." If "606" is to become a substitute for mercury it must be judged on its own merits. An adjuvant is a different matter, and as such salvarsan, according to the literature, appears to have a definite place in selected cases, mainly in those in which iodide of potassium was formerly used. The almost universal trend of opinion now is that salvarsan is not to be considered a substitute for mercury in average cases of early syphilis. The effect of this drug on induration in the chancre and the induration in the lymphatic glands is reported by numerous observers to be slight and not nearly as marked as with mercury. Such induration and enlarged glands are the repositories of syphilis, and, if not thoroughly reduced, relapse is usually ensured. The therapeutic action of salvarsan may be

brilliant, but the effect is temporary judging by clinical reports and the evidence of the Wassermann reaction. In parasyphilis salvarsan is of little avail, judging by published opinions. In certain ulcerative conditions, in malignant, laryngeal, and tertiary syphilis, salvarsan is valuable, also in mutilating syphilis where phagedæna attacks the lesions, or in persons suffering from mercurial poisoning resulting from injudicious administration.

Comparative Toxicity of Action.

In a recent review on the "Experimental Chemistry of the Spirilloses"[12] it is stated: "We have for a long time had in mercury a specific remedy for syphilis, but a great disadvantage consists in its intense toxicity in relation to curative action." Is this impeachment of mercury fair, is it true?

As regards relative toxicity of action, there are 35 recorded deaths under salvarsan quoted in English literature[13] in a period of a little over a year. Dr. Levy Bing informed me of two other deaths under salvarsan in Paris in the week preceding my arrival, and four deaths previously, none of which had as yet been published. They did not occur amongst persons *in extremis*, but, I gather, amongst otherwise healthy adults. He is of opinion that the total number of deaths under salvarsan probably amounts to 70 or 80 persons.

Intravenous mercurial injections were introduced in 1864 by Scarvenzio and gave rise to some toxic signs, including death, and for this reason were discontinued. In a recent book on salvarsan Mr. J. E. R. McDonagh states that under mercurial injections the deaths number 70. The cases, however, are not quoted or the references given; I can only trace 26 under intramuscular mercurial injections.[14] These deaths under mercury date from 1864 and occurred over a period of nearly 50 years in a much larger number of cases. The toxicity of salvarsan, therefore, would appear to be at least equal to, if not greater than, that of mercury, quite apart from other recorded toxic signs. In the British Pharmacopœia both are classed amongst the poisons.

The occurrence of cancer after the use of arsenic was recently brought forward by Sir Jonathan Hutchinson. This is at present *sub judice*. One drawing on the table from the College Museum shows an extensive dermatitis and so-called psoriasis directly due to arsenic.

The question arises whether salvarsan, the most recent organic preparations alike atoxyl, is decomposed in the system into inorganic arsenic. Dr. J. M. Fortescue-Brickdale (lecturer on pharmacology, Oxford) states: "In man the excretion of atoxyl usually amounted to 50 to 90 per cent. within nine hours, partly as atoxyl and partly in another form, the latter being

found in the urine for several days. The atoxyl retained in the body is to some extent decomposed, so that after a sufficiently long time enough inorganic arsenic is formed to produce the ordinary toxic symptoms. When atoxyl is applied to the treatment of syphilis, chorea, or any of the grave forms of anæmia, there is no evidence that any further action takes place than can be ascribed to the gradual splitting off of inorganic arsenic, and thus no advantage is gained in giving a rapidly eliminated form in large doses rather than one which, being slowly excreted, can be given in small ones."

I have used in selected cases of syphilis Donovan's and Fowler's inorganic arsenical preparations by the mouth for 18 years with great success. Others testify to their value, and they have existed in the British Pharmacopœia for 50 years. They are apparently less toxic, as no death is known. They are most valuable in late secondary or tertiary manifestations, and in cases where malaria exists in association with syphilis. Sanatogen, which is organic phosphorus, is also valuable in severe and malignant syphilis, and causes a rapid gain of weight, when cases previously unbenefited by mercury or potassium iodide rapidly improve, and these drugs can then be given with advantage.

Mr. Ernest Lane has drawn attention to certain difficulties in the technique which occurred with intravenous mercurial injections. These, no doubt, can be obviated, but the veins may be friable in syphilis, and in one instance that I saw the entry was only made after 11 attempts on the veins of both arms by an experienced man.

Some Canons regarding Results of Treatment.

In forming an opinion on the relative value of different drugs in treating syphilis the following canons may prove useful: First, the drug must be tried alone and judged on its own merits. Secondly, the manifestations of early syphilis, more especially induration in the chancre, must be removed in four to six weeks, and glandular enlargements, when they exist, must be rapidly reduced in three months from contagion. Mercury can do this. Thirdly, the result of the Wassermann original reaction should be recorded at three, six, and nine months, if this test when the technique is standardised is later accepted as conclusive evidence of syphilis. Fourthly, the recurrence of symptoms or relapse within the first 6-12 months from contagion must be noted, bearing in mind that a large number of cases of syphilis are often very mild and may not relapse even with an entire absence of treatment until parasyphilis occurs. Fifthly, the later occurrence, or otherwise, of

tertiary manifestations and parasyphilis recorded. Sixthly, the mortality.

Before discussing some general considerations I draw your attention to some drawings of yaws on the table. This is a disease closely simulating syphilis, but due to a different spirochæta. In connexion with remarks in my first lecture on the varieties of spirochætæ found in primary syphilitic chancres, it is possible that we may find different types of syphilis due to other spirochætæ, just as varieties of trypanosomes are found.

Observations on Treatment.

As far back as 1786 John Hunter condemned "the ungrateful and unsettled mind of man" in his endeavour to obtain a substitute for mercury in the treatment of syphilis. He wrote: "If there is such a thing as a specific, mercury is one for the venereal disease . . . . yet mankind are in pursuit of other specifics for this, as if specifics were more common than disease."[15] If for the word venereal we substitute early syphilitic disease, then Hunter's words are as true to-day as at the date when they were written. In amplification of Hunter's words the following facts require consideration before we lightly dismiss mercury in favour of arsenic. The grave effects of syphilis are largely due to the original intensity of infection, to personal susceptibility to the action of the virus from lowered general health, to racial susceptibility, to intemperate habits, to the neglect of early treatment, and to the injudicious use of mercurial preparations. The primary and early secondary stages run a definite course, and no line of treatment can absolutely prevent the evolution of manifestations, but good treatment in hospital in the early stages markedly ameliorates the general blood condition.

Owing to our ignorance of the laws of assimilation and elimination, it is unwise to give the patient in any stage as much mercury as he can stand, because this practice, though advocated by some persons, constitutes an abuse of the drug. This may result in mercurial stomatitis, or mercurial stasis and poisoning, from at first being unduly accumulated and later too suddenly eliminated. This would also affect the general health, which is a most important consideration, as the manifestations of syphilis are usually in inverse ratio to it. Treatment should, I think, be directed towards enabling the patient to take the drug by regulating elimination, and inducing an increase of metabolism by baths, food, and general exercise in the fresh air. If the bactericidal properties in the blood are to effect the cure of syphilis, this must necessarily result from increased metabolism due to the careful administration of mercurial or other preparations. As a result of such adminis-

tration the lymphatic glands become reduced in size, and so continue their depurative and eliminatory function. When this fails they break down and suppurate. This result is not infrequently seen in neglected or badly treated syphilis. Too long a continuance of a large dose in any form creates a markedly retrograde effect, and gives rise to anæmia, loss of weight and general condition, as well as acting as a systemic poison, and it probably prevents antibodies forming in the blood. The factor "general condition," when adequately maintained, has no doubt as powerful an effect as the mercury in improving the status of the red blood corpuscles, and in eliminating the syphilis by improving the tone of eliminating organs, such as the liver, kidneys, and skin. "If blood counts be made it will be found that the count of red cells and the amount of hæmoglobin increase during the first three weeks of mercurial treatment begun when secondary manifestations of syphilis have occurred. After that time if mercury is still given the hæmaglobin and, later, the number of red corpuscles begin to decline."[16] Hydrotherapeutics and electro-therapeutics are useful adjuncts to a mercurial course, and a valuable complement after it.

Before iodide of potassium is administered the question of renal sufficiency should be adequately gauged. If albumin is present or the quantity of urine is insufficient the iodide eruptions are likely to occur, and hence the value of free dilution of the drug together with hot-air or electric-light baths. These exercise a markedly beneficial effect on the kidneys and assist elimination by the skin. The headache and osteocopic pain of early syphilis may rapidly yield to potassium iodide alone or in combination with mercury, and a pustular syphilitic rash is markedly benefited. The drug may give rise to headache if albumin is present in the urine. Potassium iodide is more obviously beneficial the further the stage from primary infection, and its use, therefore, is imperative in the late secondary and tertiary stages or in any manifestations, however early, such as malignant syphilis presenting the attributes of those stages. This drug is most valuable in cases of early syphilitic orchitis, in periostitis, nodes, gummata, gummatous ulcerations, and in threatened brain or cord lesions. Patients who are intolerant of small doses, such as gr. v., may take a larger one with impunity. The drug is best borne about an hour after meals in dilute solution in such vehicles as water, milk, and sarsaparilla. The depressant action is best avoided by prescribing it for short periods of 10 to 14 days at a time, and in solution with ammonia carbonate, and by administering the large dose at bedtime and avoiding its use in the early morning. It is then not so likely to derange digestion or cause depression. A course of a month once a year is valuable as a precautionary measure against parasyphilitic affections,

and is strongly advocated by Sir William Gowers. The drug, as a matter of routine, should always be given as the complement of the mercurial course, since it is generally believed to assist in the gradual elimination of the accumulated mercury, and so guard against mercurial stasis and poisoning. It should not be given when mercurial poisoning has actually occurred. It also acts, especially when combined with sarsaparilla, by relieving the liver and kidneys, which may be chronically congested or lardaceous. Potassium iodide can remove the barricades of nascent fibrous tissue in which the syphilitic virus or its toxin is no doubt lodged in latent and later stages, and thus permits the leucocytes to enter and effect the removal of the virus or its products, and this explains the lessened anæmia of the patient in suitable cases. The drug often rapidly reduces the enlarged glands, and its moderate use, therefore, causes a more healthy tone of tissues, blood, lymphatics, and organs, which can then more naturally overcome the localised effects of the spirochæta. In certain stages of threatened brain syphilis which have been neglected in the early stage mercury may prove more valuable, but commonly in "syphilis grave" or in "malignant" syphilis mercury may prove quite useless, and general condition is the first consideration.

Quinine in dilute acid solution is often most valuable precedent to, or after, the first mercurial course in cachectic cases. Whether it exerts a specific action on the treponema palladium as on the malarial parasite is uncertain, but I always temporarily substitute it for mercury if there is an associated malarial history or if syphilitic fever is present. As early syphilis is associated with a loss in numbers of the red blood corpuscles and in the amount of hæmoglobin in these cells, quite possibly its chief action may be in overcoming the degenerative action, and thus assisting the blood to deal with the inroads of the virus in the early and more remediable phases of the disease by an increase in its phagocytic power or by the formation of antibodies. Cod-liver oil and iron are similarly valuable for their hæmatinic powers. Any drug, however, or any means which tend to reduce the number of spirochætæ in the system in the early stages, will consequently lessen the amount of toxin produced which can later injure the central nervous system and give rise to parasyphilitic affections.

The very greatest advantage may accrue from a cessation of mercury or potassium iodide and the substitution of other tonic remedies. I think that this is more especially the case in alcoholic, scorbutic, anæmic, malarial, or tubercular subjects, and in malignant syphilis. There is no class of disease in which the beneficial results of judicious and early treatment are so marked as in syphilis. If the remedy used is doing good the

result is early apparent and the manifestations of the disease disappear; if, on the contrary, the manifestations are stationary or growing progressively worse the remedy is inadequate and fresh methods should be essayed, either by an increase or decrease of dose or the substitution of other drugs and remedies. If there are ulcers in the throat or mouth local treatment is requisite, and a minced meat or stew diet is essential to successful results. Otherwise the patient tends to lose weight if he is unable to masticate or swallow too solid food, and mercury would only aggravate matters. Success more often depends on maintaining the strength by the judicious use of stimulants and nutritious food than on drugs. This is especially true in cases of iritis, severe throat lesions, necrosis of bone, and in malignant syphilis.

Prophylaxis.

Coming to the important question of prophylaxis, there are two essentially different modes of State intervention. First, the system known as Regulation, which implies registration and attendance. The second mode is "to require doctors and others to notify all cases of actually existing disease in persons of whatever class or sex to the health authority, who inquires into the means of segregation and treatment (as in the case of other infectious diseases) and is empowered to remove the patient to hospital if necessary." In the case of poor persons this implies a certain outlay for hospital accommodation and food, but it pays the State a hundredfold. Notification is not unequal between men and women, nor does it unduly encourage immorality. Inquiries extending over 20 years in Brussels elicited the fact that amongst 1523 out of 3505 women the primary cause of prostitution is poverty. If, therefore, prostitution is mainly dependent on poverty, and it is impossible to remove the latter, prostitution must be supervised. The late Dr. Parkes said: "In the case of venereal diseases the State must as much protect its citizens as from the danger of foul water or the risks of any other perilous and unhealthy trade."

I have outlined elsewhere the prevalence and some of the fundamental facts on which the "control of venereal diseases at their sources in civil communities" is dependent.[17] It is merely desired to point out now that in India, where control has existed since 1897 under the Cantonment Act, venereal diseases have steadily decreased year by year in the 70,000 British troops always stationed there amongst a native population of 300 millions. In 1895 in India the admissions to hospital for all forms of venereal disease reached the enormous total of 537 per 1000 of strength. In 1908 the admission-rate was only 70 per 1000, and yearly less since. In 1897 there

were 661 invalids from India to England for venereal disease, and in 1908 only 59 invalids.[18] In 1895 there were over 3000 soldiers (three regiments) constantly sick in hospital with venereal diseases; and in 1908 only 500. This is an enormous saving in men and money, as a trained soldier landed in India costs the State £100. Coming to the civil aspect in England, a Royal Commission on the Blind, the Deaf, and the Dumb, which reported to both Houses of Parliament in the year 1889, estimated that about 7000 persons in the United Kingdom had lost their sight from ophthalmia neonatorum, and assessed the cost to the State for these cases of preventable blindness at £350,000 a year. This disease is recently notifiable. Syphilis is directly responsible for about 12 per cent. of all male admissions to lunatic asylums. This is independent of the cost of maintaining cases in workhouses and infirmaries.

When quite a young man I expressed the view that it was quite feasible to stamp out syphilis if the necessary measures were taken.[19] The ideal of my youth has borne fruit in my old age. At Malta freshly contracted syphilis has been practically stamped out during this year, and recently soft chancres very nearly so. In the year 1911 to date there have been only three or four cases of freshly contracted syphilis amongst troops at Malta. In 1909 there were 87, and in 1910 35 freshly contracted cases. There is only one "venereal sore" case at present in hospital. The troops number 7000. An equal number of sailors of the Royal Navy arrive periodically, and the population of the island is a quarter of a million persons. It is not proposed to weary you with statistics, but merely to mention how this has been done: (1) Confidential notification applied to both sexes; (2) segregation of diseased men and women in hospital in the early contagious period of disease for a few weeks; and (3) prophylaxis by efficient in-patient and later out-patient treatment.

You will say, "Ah! but the clandestine—how do you control her? It is she, and not the professional prostitute, who spreads syphilis five times out of six." This may be so in large cities, and it is very difficult to control, but this is an insufficient reason for doing nothing. No one asks for the Contagious Disease Acts to be reapplied to 12 towns in England, but common sense in dealing with these matters would appear to suggest that some form of public health control should be exercised in all towns, since the disease in question is worse than small-pox. The following are very practical suggestions:—

1. Rigid suppression of solicitation in the streets by women, or by men, who act as middlemen and finance the situation, or live on the earnings of women. Police action is possible under the Town Clauses Act of 1847. The Act is applied in London,

and the police have power to arrest persons soliciting without the person solicited being called on to give evidence.

2. The prostitution of girls under age should be suppressed. At the St. Lazare Hospital, Paris, minors are separated from the elder women in the wards and in the chapel.

3. Complete and compulsory courses of instruction in venereal diseases should be instituted in every university so as to ensure the training of really competent practitioners.

The foregoing were among the main recommendations of an International Conference in Brussels in 1899.

In conclusion, the St. Lazare Hospital, Paris, built in 1683, first convent, then prison, now part hospital, part prison, has 1000 beds for the lower classes of diseased prostitutes. There is a life-size, gruesome picture over the chapel entrance of a dead prostitute being carried out in solemn state for burial. The picture, no doubt, is placed there to remind those who enter that "The wages of sin is death." The Scriptural reading, however, appears more humane, "Let him who is without sin cast the first stone."

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